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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,061	11/16/1999	JOSEF ENDL	P564-9035	3812

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EXAMINER
VANDER VEGT, FRANCOIS P

ART UNIT	PAPER NUMBER
1644	20

DATE MAILED: 06/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/441,061	Applicant(s) ENDL ET AL.	
	Examiner F. Pierre VanderVegt	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 8 April 2003

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 46-58 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 46-58 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 08 April 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

Claims 1-45 and 59-79 have been canceled.

Claims 46-58 are currently pending and are the subject of examination in the present Office Action.

1. In view of applicant's amendment filed April 7, 2003, only the following grounds of rejection are maintained for the reasons made of record.

Claim Rejections - 35 USC § 112

2. Claims 46-58 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

It was previously stated: "The instant claims are drawn to a complex or pharmaceutical composition thereof, wherein said complex comprises a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said peptide or peptide derivative has a length of at most 25 amino acids and comprises (a) a peptide of at least 6 amino acids of SEQ ID NO:2, or (b) a peptide or peptide derivative having a length of 6-25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of peptide (a) and includes anchor positions for binding to alleles or peptide binding derivatives of MHC Class II molecules DR3 or Dr4.

The instant disclosure of a complex comprising a "a peptide of at least 6 amino acids of SEQ ID NO:2" and "a peptide or peptide derivative having a length of 6-25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of peptide (a)" and "an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4" does not adequately describe the scope of each claimed genus, each of which encompasses a substantial variety of subgenera. The instant specification describes no derivative or fragment of the amino acid sequence consisting of SEQ ID NO: 2, which consists of 25 amino acids. Further there is inadequate written description for the recitation of the limitation that said peptide includes anchor positions for binding to alleles or peptide-binding derivatives of MHC Class II molecules DR3 or DR4, because there is no description of the required anchor resides which make up the Class II binding motif of said peptides, such as the specific number and specific position of said anchor residues, within a peptide, or such as which specific amino acid can suffice in which specific anchor positions. It is noted that US-PAT-NO: 5489742 teaches that at least eight subtypes of the alloantigen HLA-DR4 have been identified, including Dw4, Dw10, Dw13.1, Dw13.2, Dw14.1, Dw14.2, Dw15 and Dw "New", (see column 3, lines 13-19). Furthermore, Rammensee et al (Immunogenetics (1995) 41:178-228) teaches that at least 4 of said haplotypes bind peptides that contain distinct sets of consensus binding motifs which contain distinct anchor residues, (see entire article, including pages 213-214). The specification does not describe the motifs for any of said Class II binding peptides, and with the exception of a peptide consisting of the amino acid sequence of SEQ ID NO: 2, the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify the polypeptides encompassed. It is noted that a description of a genus of cDNAs may be achieved by means of a recitation

of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly&Co.*, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Therefore, based on the instant description of only one peptide, (a peptide consisting of the amino acid sequence of SEQ ID NO: 2) and no description of the requisite number, position and identities of anchor residues of the claimed genus of peptides, the structure of a complex or pharmaceutical composition thereof, wherein said complex comprises "a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said complex comprises peptide or peptide derivative having a length of 6 to 25 amino acids, which exhibits a specificity or/and affinity which is essentially equivalent to that of the peptide of at least 6 amino acids of SEQ ID NO:2, and includes anchor positions for binding to alleles or peptide-binding derivatives of MHC class II molecules DR3 or DR4", is not conventional in the art and one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus of said complex comprising said peptides encompassed by the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) "

Applicant's arguments filed April 8, 2003 have been considered but are not persuasive. Applicant had amended the claims to recite four MHC Class II molecules to which the peptide of the invention may bind and to recite that a peptide derivative must be at least 50% homologous to a selected GAD peptide and asserts that the amendment obviates the ground of rejection. The Examiner respectfully disagrees with Applicant's assessment. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (MPEP 2163 II.A.3a.ii.). In the present application, this requirement is not met, as a mere recitation of four MHC haplotypes and 50% homology to portions of SEQ ID NO: 2 in the specification and claims does not convey possession of the claimed invention, as the genus still encompasses a sizable number of derivatives between 10 and 25 amino acid residues in length and no guidance in regard to which residues should or should not be changed to preserve any particular function.

3. Claims 46-58 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a complex comprising a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said complex comprises "a peptide consisting of the amino acid sequence of SEQ ID NO: 2, and includes anchor positions for binding to alleles or peptide-binding derivatives of MHC class II molecules DR3 or DR4, does not reasonably provide enablement for the broader recitation of a complex comprising any peptide or any peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said complex comprises any peptide or any peptide derivative having a length of 6 to 25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of the peptide of at least 6 amino acids of SEQ ID NO:2, and includes anchor positions for binding to alleles or peptide-binding derivatives of MHC class II molecules DR3 or DR4". The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in the instant claims without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with respect to the extremely large number of peptides broadly encompassed by the claims.

It was previously stated: "The instant claims are drawn to a complex or pharmaceutical composition thereof, wherein said complex comprises a peptide or peptide derivative derived from glutamic acid decarboxylase which is bound to an allele or a peptide-binding derivative of MHC Class II molecules DR3 or DR4, wherein said peptide or peptide derivative has a length of at most 25 amino acids and comprises (a) a peptide of at least 6 amino acids of SEQ ID NO:2, or (b) a peptide or peptide derivative having a length of 6-25 amino acids which exhibits a specificity or/and affinity which is essentially equivalent to that of peptide (a) and includes anchor positions for binding to alleles or peptide binding derivatives of MHC Class II molecules DR3 or DR4.

The instant specification discloses no derivative or fragment of the amino acid sequence consisting of SEQ ID NO:2, which consists of 25 amino acids. It is noted that the instant claims recite the limitation that said peptide or peptide derivative, includes anchor positions for binding to alleles or peptide-binding derivatives of MHC Class II molecules DR3 or DR4. However, the specification does not teach the motifs for any of said Class II binding peptides. Ramensee et al (Immunogenetics (1995) 41:178-228) teaches the class II binding motifs of 4 DR4 haplotypes (see entire article, including pages 213-214). However, it is noted that US-PAT-NO: 5489742 teaches that at least eight subtypes of the alloantigen HLA-DR4 have been identified, including Dw4, Dw10, Dw13.1, Dw13.2, Dw14.1, Dw14.2, Dw15 and Dw "New", (see column 3, lines 13-19). Therefore there are several peptide motifs, known and unknown, that have not been disclosed. Therefore, it would require undue experimentation for one of skill to predict which peptide fragments and peptide derivatives of SEQ ID NO:2 could bind DR3 or DR4, without further guidance and direction regarding the peptide binding motifs required by the numerous alleles of DR3 and DR4. Further, it is noted that Rammensee et al (Immunogenetics (1995) 41:178-228) teaches that at least 12 amino acids are generally necessary to provide the essential motif for peptide binding to MHC Class II molecules (see entire article, including page 183, column 2). The instant claims all encompass complexes comprising peptides which have less than 10 amino acids. Therefore it would require undue experimentation to predict which peptides sequences of which length would bind DR3 or DR4, with the exception of a peptide consisting of the amino acid sequence of SERQ ID NO:2, without further guidance and direction from the instant specification.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention."

Applicant had amended the claims to recite four MHC Class II molecules to which the peptide of the invention may bind and to recite that a peptide derivative must be at least 50% homologous to a selected GAD peptide and asserts that the amendment obviates the ground of rejection. The Examiner respectfully disagrees with Applicant's assessment. It is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. The specification does not appear to provide sufficient guidance as to which residues should or should not be changed to preserve any particular function. The variation permitted by the instant claim language is extensive. Consequently, the experimentation left to those skilled in the art to determine which "variant" sequences would still result in polypeptides having the same function as the GAD polypeptides disclosed in the specification as filed is unnecessarily, and improperly, extensive and undue.

Conclusion

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (703) 305-4441. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096

OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014.Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
June 24, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
RECH CENTER 1600
6/26/03